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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,699	06/14/2002	Ikuo Nishimoto	082376-000000US	2315

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,699	NISHIMOTO, IKUO	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed June 18, 2004. Amendments were made to the claims. Specifically, new claims 14-19 were added.

Claims 1-19 are pending in the instant application. Claims 3 and 9 remain withdrawn as being drawn to a non-elected invention. Claims 1, 2, 4-8 and 10-19 are under examination in the instant application. Any rejection of record in the previous Office Action, mailed February 12, 2004, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. **This rejection is necessitated by amendment of the claims.**

Applicant suggests that support for the addition of the limitation "(d) cross-hybridizing the nucleic acids to each other to identify non-redundant groups" is located at page 37, lines 8-24 of the instant specification. However, the specification does not mention performing cross-hybridization with respect to the identification of disorder suppressors for any condition, only with respect to Alzheimer's disease; this is not commensurate in scope with the broad range of disorders set forth in the claimed method, thereby representing new matter with respect to performing that step with regard to any disorder. Furthermore, the specification does not suggest doing this procedure with regard to any disorder at any other location in the specification, or in a general context. As such, this step is considered to represent new matter with respect to the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8 and 10-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection that is necessitated by amendment.**

Claims 1, 8, 16 and 17 (and their dependent claims) recite the phrase "obtained from an organ affected by the disorder." This phrase renders the claim indefinite because it is unclear what is encompassed within the limitation of an organ that is "affected by a disorder." For example, when someone contracts a terminal disease, the end result is death of the organism and the organs contained within the organism; in this sense, all of the organs in the organism are "affected by a disorder." Thus, the skilled artisan would be unclear as to whether or not the

claim limitation reads on all organs, specific organs as it relates to specific diseases, an organ that contains the pathological element causing the disease, etc. As such, the claim limitation is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8, and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Giambarella (cited in the previous Office Action). **This rejection is maintained for the reasons set forth in the previous Office Action, and is now applied to newly added claims 14-17.**

Claims 1, 2, 4-8, and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Guo (cited in the previous Office Action). **This rejection is maintained for the reasons set forth in the previous Office Action, and is now applied to newly added claims 14-17.**

As it relates to the application of the rejections to newly added claims 14-19, it is noted that both Guo and Giambarella concern the suppression of diseases associated with neurodegeneration (Alzheimer's disease) and with regard to the organ from which the nucleic acid was obtained (described in more detail in the arguments below). Because both Guo and Giambarella teach these elements, the newly added claims are included in the rejection as set forth previously.

Response to Arguments Concerning Claim Rejections - 35 USC § 102

Applicant's arguments filed June 18, 2004 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal as it relates to both the rejections in view of Guo and Giambarella, which will be answered simultaneously:

1. It is alleged that both references lack an element of the claims because neither reference contains the limitation where the nucleic acid is "obtained from or synthesized from a nucleic acid obtained from a tissue of an organism suffering from a disorder that accompanies cell death, wherein the tissue is obtained from an organ affected by the disorder" (see for example page 12, first full paragraph of Applicant's Response).

2. It is alleged that neither reference makes the instant claims obvious, and indeed teach away from the instant claims, because they suggest "expression of a specific gene with a known biochemical activity that counteracts a cell death-associated pathway is the way to identify genes that attenuate cell death." It is further indicated that neither teaching "would have motivated a practitioner to make a cDNA library using a tissue sample from an organ affected by a cell death disorder," etc. (see for example page 13, first full paragraph of Applicant's Response).

3. It is alleged that the instant claims are diametrically opposed to the teachings of Giambarella and Guo because they "do not require *a priori* knowledge of the identity or function of genes" obtained from a source. Example 1 of the instant specification is then recited in support of this conclusion (see for example page 14, last paragraph of Applicant's response).

Applicant's arguments have been considered but are not found convincing for the following reasons:

1. It appears that certain terms of the claims are being improperly interpreted in a more narrow sense than they must be read in view of the teachings of the instant specification. This is particularly important with regard to the argument that neither Guo nor Giambarella teaches a nucleic acid coming from a tissue of an "organism suffering from a disorder." The instant specification defines the term "organism suffering from a disorder" as including organisms "*who have not yet developed visible clinical symptoms but carry factors (or elements) that cause the disorder*" (emphasis added) on page 8, lines 25-27. As such, the source of a nucleic acid administered in the instant claims can be obtained or synthesized from a nucleic acid that comes from a *normal cell* originating from a *normal tissue* obtained from a *non-symptomatic organism*, so long as the organism comprises a tissue that carries at least one factor (or element) that contributes to a disorder. In this specific instance, this limitation is met by both the Guo and Giambarella references.

According to the definition of an "organism suffering from a disorder" as set forth in the specification, the source organism needs only to harbor a tissue that contains a factor (or element) that causes a disorder in order to meet the limitation of the claim. All mammals (e.g., mice, rats humans, etc.) contain neural tissue (e.g., brain tissue). It is accepted that the α-synuclein gene is causally involved in the emergence of Parkinson's Disease, and this is recognized by the instant specification (see for example page 2, lines 7-10). It is also known that α-synuclein is normally expressed in neuronal tissue, thus normal brian tissue "contains a factor (or element) that causes a disorder. A similar scenario exists regarding Alzheimer's Disease,

which is believed to be induced by a few different genes such as the presenilins, which are also expressed normally in neuronal tissue. Thus, any nucleic acid coming from the neuronal tissue of any organism necessarily comes from a tissue that "contains a factor (or element) that causes a disorder," and thus such a nucleic acid would necessarily meet the new limitation in the instant claims. Thus, one must consider the source of the nucleic acids used by Guo and Giambarella when determining whether the nucleic acids originate from a tissue of an organism suffering from a disorder that accompanies cell death (i.e., the tissue of any organism).

The nucleic acid used by Giambarella encodes βARK1, as provided by RJ Lefkowitz, as pointed out by applicant in their arguments on page 12 of the response. However, the original source for the nucleic acid provided by RJ Lefkowitz was from a rat brain (an organ that is directly affected by Alzheimer's Disease), as evidenced by the teachings of Arriza *et al.* (*J. Neuroscience* **12**: 4045-4055, 1992; see entire document, especially the Abstract and Materials and Methods; it is noted that this reference is provided only as evidence concerning the source of the nucleic acid used in the anticipatory reference, and is not a part of the rejection itself). Thus, the source of the nucleic acid used by Giambarella was a rat brain tissue; according to the definition of "organism suffering from a disorder" in the instant specification, rat brain tissue contains a factor (e.g., presenilin or α-synuclein) that causes a neurodegenerative disease associated with cell-death (Alzheimer's Disease or Parkinson's Disease). As such, the nucleic acid used by Giambarella meets the limitations as amended, contrary to the arguments provided in response to the rejection.

The nucleic acid used by Guo encodes calbindin-D28k which, according to Applicant, had an indeterminable source. As such, the Office determined the first cloning of the calbindin-

D28k gene, which would serve as a template for the synthesis of other calbindin-28k genes, absent evidence to the contrary. The initial cloning of calbindin-D28k was from a cDNA library established from mouse cerebellar tissue, evidenced by the teachings of Nordquist *et al.* (*J. Neuroscience* **8**: 4780-4789, 1988; see entire document, especially the Abstract and Materials and Methods; it is noted that this reference is provided only as evidence concerning the source of the nucleic acid used in the anticipatory reference, and is not a part of the rejection itself). Thus, the source of the nucleic acid used by Guo was a mouse brain tissue (an organ that is directly affected by Alzheimer's Disease); according to the definition of "organism suffering from a disorder" in the instant specification, mouse brain tissue contains a factor (e.g., presenilin or α-synuclein) that causes a neurodegenerative disease associated with cell-death (Alzheimer's Disease or Parkinson's Disease). As such, the nucleic acid used by Guo meets the limitations as amended, contrary to the arguments provided in response to the rejection.

Given the broad definition of an "organism suffering from a disorder" as set forth in the specification, and the original sources of the nucleic acids used by the Guo and Giambarella references, the argument that Guo and Giambarella do not teach a nucleic acid that is "obtained from or synthesized from a nucleic acid obtained from a tissue of an organism suffering from a disorder that accompanies cell death, wherein the tissue is obtained from an organ affected by the disorder" appears invalid. As such, the argument is unconvincing and the rejection is maintained.

2. First, it is reiterated that the instant rejection is under 35 USC § 102, thus there is no question of obviousness to perform the claimed method. Rather, it is simply a question as to whether or not the cited references perform a method that falls within the limitations of the claims. As set

forth in the previous Office Actions and as clarified in response to Applicant's arguments regarding the limitation where the nucleic acid is "obtained from or synthesized from a nucleic acid obtained from a tissue of an organism suffering from a disorder that accompanies cell death, wherein the tissue is obtained from an organ affected by the disorder," the instant claims are anticipated by the Guo and Giambarella references. The argument that both Guo and Giambarella teach away from the instantly claimed invention because they 'suggest expression of specific genes with specific activities' and 'do not teach making a cDNA library according to the instant specification' are irrelevant because none of the instant claims contain these limitations. It appears that Applicant is reading limitations into the claims when they are not expressly set forth in the claims, and then basing an argument on these non-existent limitations. As such, the rejection is maintained.

3. The instant claims do not excluded having "*a priori* knowledge of the identity or function of genes" prior to using them in a method. Thus, it again appears that Applicant is reading non-existent limitations into the claim in order to suggest that Guo and Giambarella teach away from the instantly claimed method. This is also true with respect to the arguments concerning Example 1 of the instant specification. The instant claims are not commensurate in scope with what is taught in Example 1 of the instant specification, and are indeed very much broader than the specific example. It is because the instant claims are so broad when read in light of the specification as it concerns the recited limitations that Guo and Giambarella anticipate the claimed invention. Thus, the arguments are unconvincing because they improperly insert limitations into the claims that are not present therein.

In conclusion, the rejections are maintained because, contrary to Applicant's assertion, the limitation on the nucleic acid used in the claim does not exclude the nucleic acids used by Guo and Giambarella given the broad definition of an "organism suffering from a disorder." Furthermore, the limitations that are allegedly not taught by Guo or Giambarella (e.g., the creation of a cDNA library, etc.) are not even limitations in the claims. For the reasons set forth in the previous Office Action, and in view of the interpretation of the new limitations set forth in the claims as clarified in section (1) above, the rejection under 35 USC § 102 in view of Guo and Giambarella is still considered proper, and is therefore maintained.

Allowable Subject Matter

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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GERRY LEFFERS
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